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Highly Selective Fluorescence Turn-On Sensor for Fluoride Detection

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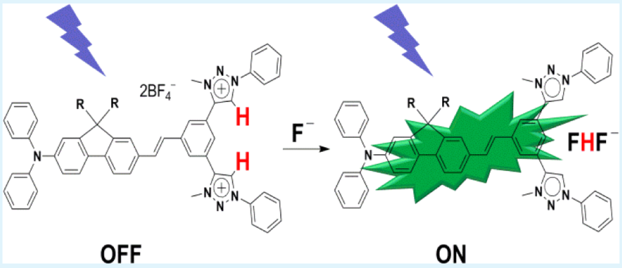
Ⓢ *Supporting Information*

ABSTRACT: Through click chemistry, triazole and triazolium groups have been explored to recognize anions through C−H···A⁻ hydrogen-bonding complexion. Herein, we demonstrate evidence of fluoride-induced deprotonation of a C−H bond and its application in fluoride detection. The combination of fluorene and triazolium units produced a highly selective fluorescence turn-on prototype sensor for fluoride. The interactions between the C−H bond and F^- were studied by fluorescence spectroscopy and ^{1}H NMR titrations. Test papers were prepared to detect fluoride in aqueous media at concentrations down to 1.9 ppm, important for estimating whether the fluoride concentration in drinking water is at a safe level.



KEYWORDS: *fluoride, fluorescence sensor, fluorene, triazolium, fluoride detection, anion sensor*

Research on receptors and sensors for anions is currently attracting much interest because of the importance of anions in environmental, biological, and chemical processes.[1−10] For human health, the role of fluoride is significant. On one hand, fluoride plays a beneficial role in treating osteoporosis and protecting dental health; on the other hand, excessive fluoride ingestion may cause fluorosis and urolithiasis.[11−13] The significance of fluoride has led to efforts to develop fluoride sensors over the past decade.[14−26] Among various sensors, fluorescence sensors are among the most attractive because of their high sensitivity and low detection limits. However, most of the reported fluorescent fluoride sensors are based on a fluorescence quenching mechanism.[23−25] Signal output discrimination with quenching is often poor at low [F^-], limiting their utility. While the current work was being completed, Castellano et al. reported an intriguing turn-on F^- sensitive stilbazolium compound.[26] Thus, the impetus for the development of fluorescence-enhanced turn-on sensors for fluoride detection is compelling.

Because of its small size and high charge density, fluoride has the highest affinity to protons among anions and the ability to deprotonate hydrogen-containing polar groups such as NH groups. This unique property makes fluoride sensors based on the deprotonation mechanism exhibit potentially good selectivity for F^- over other anions, especially CN^-, AcO^-, and $H_2PO_4^-$, which usually exhibit harmful interference in detecting fluoride with hydrogen-bonding based fluoride sensors.[27−31] Therefore, fluoride sensors containing NH groups such as urea,[29] sulfonamide,[28] pyrrole,[24,31] and imidazole,[30] have been designed and synthesized to detect fluoride. However, it is a challenge to employ C−H bond deprotonation for fluoride detection because of the low acidity of the C−H bond.

In recent years, with the development of click chemistry, C−H bond containing groups such as triazole,[32−35] imidazolium,[36,37] and triazolium[38−41] have been incorporated in anion recognition. All these anion receptors are based on C−H···A hydrogen-bonding interactions. Cao et al.[40] tried to attribute the problem they recently encountered to the deprotonation of the C−H bond by fluoride, but no evidence was provided to substantiate it. To the best of our knowledge, no C−H bond deprotonation-based anion sensor has been reported thus far.

Herein, we report a highly selective and sensitive fluorescent fluoride sensor **1**, a fluorene derivative bearing two triazolium groups (Scheme 1). Sensing is based on deprotonation of the C−H bond, displaying "off−on" changes in its fluorescence emission upon the addition of fluoride ion. The synthetic route of sensor **1** is shown in Scheme 1. Compound **2** was synthesized via a Sonogashira coupling reaction of 3,5-dibromobenzyl alcohol with trimethylsilylacetylene. It was desilylated with KF to form compound **3**, which was then converted to compound **4** with thionyl chloride. Phosphonylation of the chloromethyl group of compound **4**, in the presence of NaI, provided compound **5**. Compounds **6**,[42] **7**,[43] and **8**[44] were prepared according to literature procedures starting with 2,7-dibromofluorene. Compound **8** was then reacted with **5** to generate **9** via a Horner−Wadsworth−Emmons reaction. Penultimate fluorene **10** was obtained from a copper(I)-catalyzed alkyne−azide cycloaddition (CuAAC) reaction between **9** and iodobenzene in the presence of NaN_3, sodium ascorbate, and N,N-dimethylethane-1,2-diamine in a solvent mixture of toluene:DMSO:H_2O (4:5:1). The target sensor **1** was prepared in a 35% yield via methylation of **10** with 2.5 equiv. of $Me_3O{\cdot}BF_4$ in anhydrous CH_2Cl_2 followed by repeated recrystallization from chloroform.

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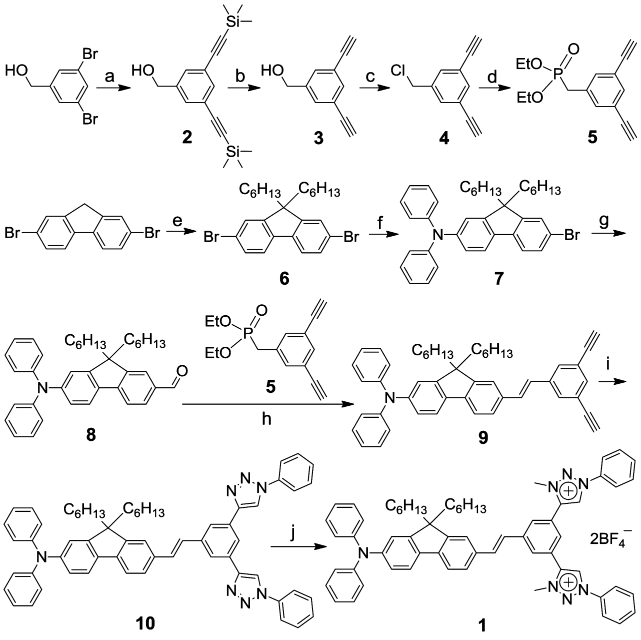
Scheme 1. Synthesis of Sensor 1[a]



[a] Reagents and conditions: (a) CuI, $Pd(PPh_3)_2Cl_2$, trimethylsilylacetylene, THF:triethylamine (4:1), reflux, 12 h; (b) KF, methanol, room temperature, 10 h; (c) $SOCl_2$, triethylamine, CH_2Cl_2, 0 °C, 30 min; then reflux, 2 h; (d) NaI, triethyl phosphite, acetone, 60 °C, 24 h; (e) 1-bromohexane, *t*-BuOK, DMF, 40 °C, 30 min; (f) diphenylamine, *t*-BuONa, $Pd(dba)_2$, dppf, toluene, reflux, 16 h; (g) *n*-BuLi, THF, −78 °C, 40 min; then DMF, −78 °C, 1.5 h; (h) *t*-BuOK, THF, 0 °C, 30 min; then room temperature, 3 h; (i) iodobenzene, NaN_3, CuI, sodium ascorbate, N,N-dimethylethane-1,2-diamine, toluene:DMSO:H_2O (4:5:1), room temperature, 2 h; (j) trimethyloxonium tetrafluoroborate, CH_2Cl_2, room temperature, 3 days.

The selectivity of sensor **1** for fluoride was first investigated through UV−vis spectroscopy by adding various anions (F^-, Cl^-, Br^-, I^-, CN^-, OCN^-, SCN^-, N_3^-, NO_2^-, NO_3^-, ClO_4^-, IO_4^-, AcO^-, HSO_4^-, and $H_2PO_4^-$, as n-Bu_4N^+ salts) to **1** in DMSO (see Figure S1 in the Supporting Information). The free sensor **1** displayed an absorption band at 398 nm. Upon adding fluoride, the absorption peak shifted to 385 nm and the absorption intensity increased, while no considerable change was induced to the absorption spectra by the addition of other anions. As the equiv. of fluoride increased, the absorption spectra changed gradually in both the maximum absorption wavelength and the absorption intensity (see Figure S2 in the Supporting Information). These results demonstrate that sensor **1** shows excellent selectivity for fluoride over other anions.

In good agreement with the findings for absorption, sensor **1** exhibited a specific emission response to fluoride. Moreover, compared to absorption spectroscopy, fluorescent emission spectroscopy is a more effective approach for fluoride sensing. The fluorescent properties of sensor **1** in the presence of various anions were examined in DMSO. Figure 1 shows the visual fluorescence response of **1** with excitation at 365 nm using a hand-held UV lamp. The free sensor **1** emitted no fluorescence. Upon adding fluoride, a striking blue-green fluorescence was observed. In contrast, no fluorescence response was found from other anions. The solution colors of sensor **1** with other anions stayed the same before and after excitation at 365 nm (Figure 1 and Figure S3 in the Supporting Information). The fluorescence emission spectra of sensor **1** with 20 equiv. of various anions were recorded with excitation at 385 nm (Figure 2). Corresponding to the results of visual fluorescence response shown in Figure 1, sensor **1** exhibited an intense emission band at 498 nm (quantum yield: 0.66) in the presence of fluoride, while no fluorescence signal was recorded from the free sensor **1** and **1** with other anions. These results indicate that sensor **1** exhibits high specificity for fluoride.

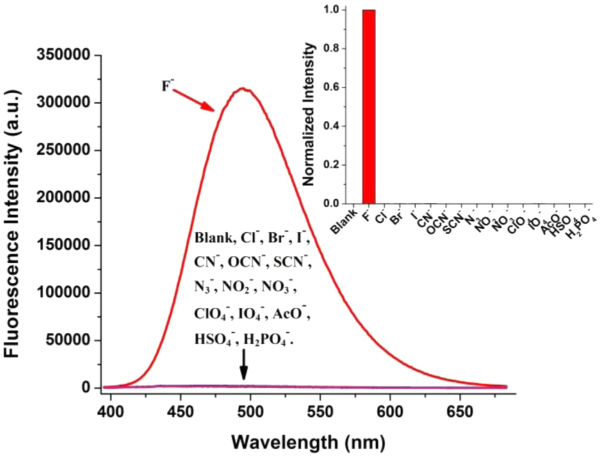


Figure 2. Fluorescence emission spectra of **1** (6.0 μM) in DMSO upon the addition of 20 equiv. of various anions (λ_{ex} = 385 nm).

To study the sensitivity of sensor **1** toward fluoride sensing, we investigated fluorescence responses of the interaction of **1** with fluoride with excitation at 385 nm in DMSO (Figure 3). As shown in Figure 3A, upon the progressive addition of fluoride, the fluorescence intensity gradually increased. Figure

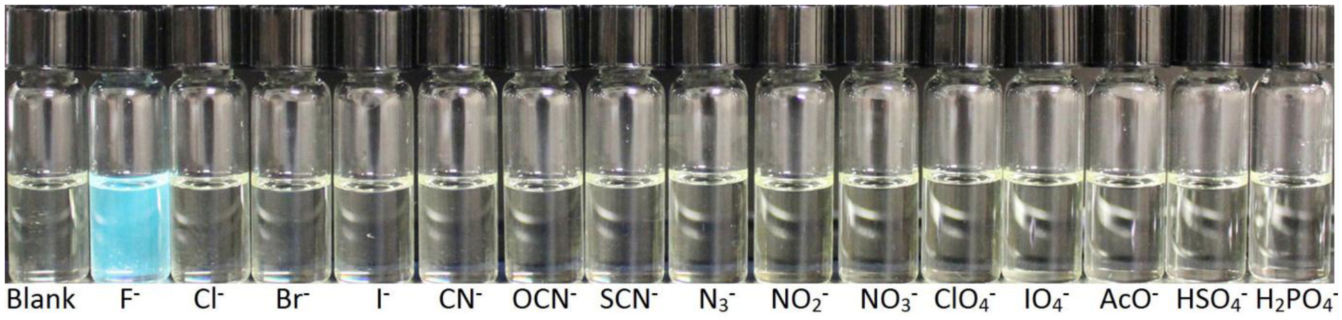


Figure 1. Visual fluorescence responses of sensor **1** (6.0 μM) in DMSO after the addition of 20 equiv. of various anions with excitation at 365 nm using a hand-held UV lamp.

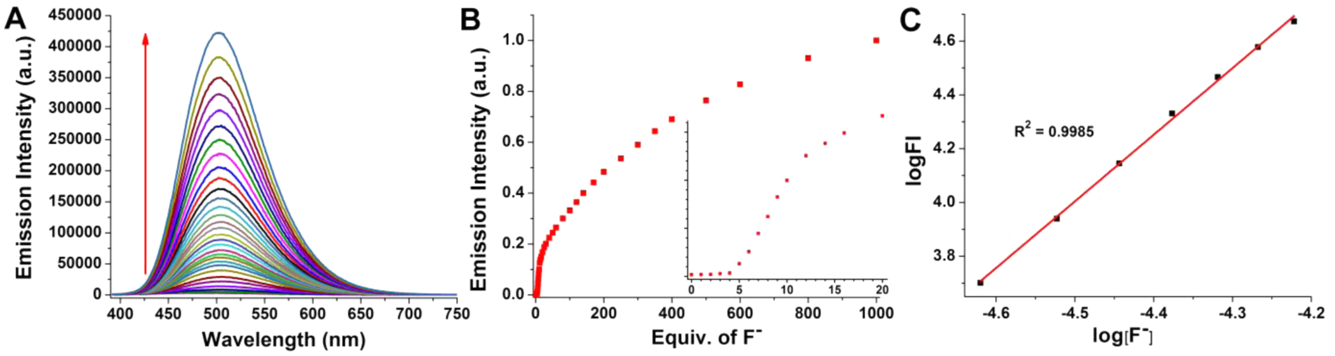


Figure 3. (A) Changes in fluorescence emission for sensor **1** (6.0 μM) upon the addition of 0−1000 equiv. of F^- in DMSO (λ_{ex} = 385 nm). (B) Fluorescence intensity as a function of added F^-. Inset: enlargement corresponding to 0−20 equiv. of F^-. (C) Plot of log FI (fluorescence intensity) versus log $[F^-]$ in the range of 4−10 equiv. of F^-.

3B illustrates the fluorescent intensity as a function of the equiv. of fluoride anions. The inset is an enlarged part of Figure 3B corresponding to 0−20 equiv. of fluoride. The first 4 equiv. of fluoride induced no fluorescence response compared to the free sensor **1**. A noticeable fluorescence emission was observed after the addition of 5 equiv. of fluoride. As more fluoride was added, the emission intensity increased with the concentration of fluoride. In the range of 4−10 equiv. of fluoride, the emission intensity increased dramatically, and after that, the rate of increase was reduced. More importantly, the plot of log(FI) (fluorescence intensity) versus log$[F^-]$ was found to be linear (R^2 = 0.9985) in this range (Figure 3C), indicating that sensor **1** can be used to determine F^- concentration.

To examine the interactions between sensor **1** and fluoride anion, we carried out ^{1}H NMR titration experiments in DMSO-d_6. As shown in the partial ^{1}H NMR fluoride titration spectra of **1** in Figure S4 in the Supporting Information, the triazolium CH proton signal (9.99 ppm) shifted downfield, decreased, and finally disappeared upon the addition of fluoride. With the disappearance of the triazolium CH signal, a significant 1:2:1 triplet signal at 16.1 ppm with coupling constant $J \approx 120$ Hz appeared after the addition of 5 equiv. of fluoride (see Figure S5 in the Supporting Information). This signal strongly suggests the formation of the bifluoride ion (FHF^-).[30,45,46] These results suggest fluoride-induced deprotonation of the CH group of the triazolium ring. This indication was further confirmed by changes in ^{13}C NMR spectra of **1** as a function of added fluoride (see Figure S6 in the Supporting Information). Moreover, based on these results and the aforementioned fact that the fluorescence response was also observed after the addition of 5 equiv. of fluoride, the observed results are consistent with the fluorescence emission originating upon the deprotonation of the C−H bond.

On the basis of the phenomena described above, we suggest a possible explanation for the interactions between sensor **1** and fluoride. Two types of interactions are involved in the process of increasing equiv. of fluoride: H-bonded complexation and deprotonation. Initial addition of fluoride generates hydrogen-bonding complexes, while further fluoride addition induces deprotonation of the triazolium groups, resulting in the formation of FHF^- and two deprotonated species, mono- and bis-deprotonated forms of **1**. Upon the addition of 1 equiv. of fluoride, a complex is formed through hydrogen bonding, exhibiting a slight decrease in the ^{1}H NMR signal of the CH proton of the triazolium ring (see Figure S4 in the Supporting Information). As more fluoride is added, the hydrogen bonding interaction between the hydrogen of triazolium CH and F^- becomes stronger, leading to a significant decrease and downfield shift in the ^{1}H NMR signal of triazolium CH proton. The results of fluorescence titration experiments demonstrated that the species formed through hydrogen-bonding are not fluorescent. With the further addition of fluoride, however, deprotonated forms of **1** are produced. When 4 equiv. of fluoride is added, monodeprotonated **1** may be formed, which emits no fluorescence. The existence of nonfluorescent monodeprotonated form of **1** explains why, after the addition of up to 4 equiv. of fluoride, no fluorescence response was observed (Figure 3). However, a very weak ^{1}H NMR signal of FHF^- was recorded (see Figure S5 in the Supporting Information). Upon adding more equivalents of fluoride, a highly fluorescent neutral bis-deprotonated form of **1** is produced. It should be noted that the neutral precursor of **1**, compound **10**, is also highly fluorescent (quantum yield: 1.0). However the methylation product of **10**, sensor **1**, bearing two positive charges (triazolium), is nonfluorescent. As a rule, cationic dyes have low fluorescence quantum yields due to greater bond length alternation character, such as in polymethine dyes; deprotonation (neutral species formation) reduces this effect, increasing fluorescence. Hence, neutral forms of this chromophore are fluorescent, whereas the fluorescence is quenched in charged species.

Encouraged by the above results, test strips of sensor **1** were prepared from filter paper to facilitate sensing F^- in an aqueous environment. As shown in Figure 4, the fluorescence of the test papers increased with the fluoride concentration of the aqueous solutions. Fluoride can be detected at concentrations as low as ca. 1.9 ppm (1×10^{-4} M). According to the EPA's (U.S.

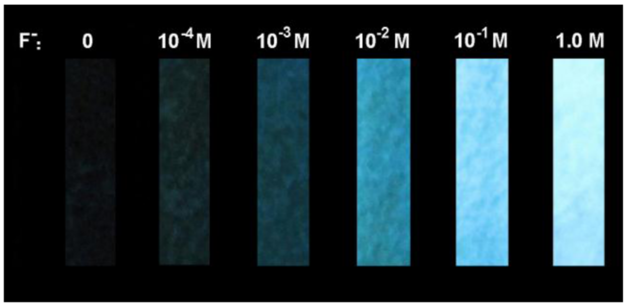


Figure 4. Fluorescence changes of test strips for detecting F^- in aqueous solution with different F^- concentrations. Irradiation at 365 nm using a hand-held UV lamp.

Environmental Protection Agency's) standards, the enforceable MCL (maximum contaminant level) for fluoride in drinking water is 4.0 ppm, and a nonenforceable secondary MCL for fluoride is 2.0 ppm. Therefore, sensor **1** test strips can be applied to effectively estimate whether the fluoride ion concentration in drinking water exceeds established standards.

In summary, the C−H bond of the triazolium ring can be deprotonated by fluoride. A novel fluorene-based fluoride sensor (**1**) bearing two triazolium groups was synthesized and characterized, which is the first reported anion sensor based on the deprotonation of a C−H bond. Sensor **1** demonstrated specific fluorescence turn-on response toward fluoride, exhibiting excellent differentiation from other anions and high sensitivity for fluoride sensing. Based on the results of fluorescence emission titration and ^{1}H NMR titration experiments, an explanation is proposed for the interactions between the bistriazolium fluorene **1** and fluoride. We expect that this interaction model will inspire the exploration of new systems for the selective detection of fluoride and other anions. Test strips based on sensor **1** were prepared and employed to detect the presence of fluoride. These may provide the basis to conveniently and inexpensively determine whether the concentration of fluoride in drinking water is below or exceeds acceptable standards.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Information on the synthesis and corresponding characterization data for compounds **1**−**10**, preparation of test strips, absorption spectra, and ^{1}H and ^{13}C spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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